AMENDMENTS TO THE SPECIFICATION

Please rewrite the first paragraph on page 11 as follows:

Preferred chromatin inactivation portions are described in the Examples, and include a polypeptide/polypeptide mimic or analogue derivable from SAP18 with the amino acid sequence (SEQ ID NO:1) XXXMAVESRVTQEEIKKEPEKPIDREKTCPLLLRVF (where XXX is, for example, a AAA or DDD linker) and a polypeptide derivable from MAD1 with the amino acid sequence (SEQ ID NO:2) XXXMNIQMLLEAADYLERREREAEHGYASMLP (where XXX is, for example, a AAA or DDD linker).

Please rewrite the first full paragraph on page 13 as follows:

Further examples of localisation portions include modified Antennapedia homeodomain based Penetratins (for example (SEQ ID NO:3) RQIKIWFQNRRMKWKK), or TAT (for example (SEQ ID NO:4) C(Acm)GRKKRRQRRRPPQC, where C(Acm) is a Cys-acetamidomethyl) or VP22 based molecules (Prochiantz (2000) *Curr Opin Cell Biol* **9**, 420-429).) or basic HIV TAT internalisation peptide.

Please rewrite the paragraph starting at 22 on pages 43-44 as follows:

As an example, the TFO is designed to form a triplex with the Interferon Stimulatable Response Element (ISRE) of the human Interferon Stimulated Gene (ISG) 6-16. (Porter A., et al., EMBO J. 7: 85-92, 1988). The ISRE is very purine rich on one DNA strand and is, therefore, a candidate sequence for forming a DNA

triplex by Höogsteen base pairing. The rules for designing potential TFO are summarised in: Vasquez KM and Wilson JH, Trends Biochem Sci, 1: 4-9, 1998. The sequence (SEQ ID NO:5) 5'-AAAGTAAAAGGGGAGAGAGGG-3' was produced as an oligonucleotide (Module 1) with an activated 5' end for chemical coupling to Module 2 peptides. Module 2 peptides explored in this study include (at least one copy of the minimal transcriptional activator domain of the Herpes Simplex Virus VP16 Transcriptional Activator protein for example the amino acid sequence (SEQ ID NO:6) GGGPADALDDFDLDMLPADALDDFDLDML or (SEQ ID NO:7) GGGPADALDDFDLDMLPADALDDFDLDMLPADALDDFDLDMLPADAL DDFDLDML-$CONH_2$ (including GGG linker)),and the human MAD1 transcriptional repressor domain (for example amino acids (SEQ ID NO:8) XXXMNIQMLLEAADYLERREREAEHGYASMLP (where XXX is, for example, a AAA or DDD linker)). The latter is a region known to interact with the histone deacetylase complex protein Sin3a. Additionally, we have explored the use of amino acids (SEQ ID NO:9) XXXMAVESRVTQEEIKKEPEKPIDREKTCPLLLRVF (where XXX is, for example, a AAA or DDD linker) of the human Sap18 protein, also known to associated with Sin3a protein. This region corresponds to a sequence of high evolutionary conservation and overlaps with a region that can mediate gene repression. Module 2 peptides were synthesised in an activated form to enable subsequent coupling to the activated Module 1 oligonucleotide by "native ligation" chemistry (see WO 01/15737 and Stetsenko & Gait (2000)

Organic Chem **65(16)**, 4900-4908), in which an N-terminal thioester-functionalised peptide is coupled to a 5'-cysteinyl oligonucleotide.

Please rewrite the second full paragraph at line 13 on page 47 as follows:

Endogenous gene regulation is measured, for example by assessing transcription of the gene (for example using PCR) or by assessing the quantity or activity of the encoded polypeptide. In an example, the oligonucleotide is directed to the Androgen receptor gene regulatory site. In particular, the oligonucleotide has the sequence (SEQ ID NO:10) 5' gggaaaggaaaagaggggaggg 3' or (SEQ ID NO:11) 5' gggaggggaaaggaaaagagg 3'.

Please rewrite the paragraph starting at line 16 on page 54 as follows:

The sequence of the ARP TFO used in this example was:

ARP TFO: (SEQ ID NO:12) (5') GFGUGGTGFGGTTGTGTT (3')

Please rewrite the first paragraph on page 55 as follows:

L217: HHHHHH-Penetratin-DDD-14aaMAD

(SEQ ID NO:13)

(Link)HHHHHHRQIKIWFQNRRMKWKKDDDMNIAMLLEAADYLE(amide)

Please rewrite the second paragraph on page 55 as follows:

L218: HHHHHH-29aaMAD-DDD-Penetratin

(SEQ ID NO:14)

(Link)HHHHHHMNIAMLLEAADYLERREREAEHGYASMLPDDDRQIKIWFQNRRMKWKK

(amide)

Please rewrite the last paragraph on pages 56-57 as follows:

RT-PCR conditions were established to give optimal sensitivity within the exponential phase of the amplification process. Total cellular RNA was isolated from the treated LNCap cells using the RNeasy Kit (Qiagen). RNA (1□g of each sample) was reverse transcribed into cDNA using the Omniscript RT kit (Qiagen). The synthesized cDNA (2□l of each sample) was subjected to PCR amplification (Qiagen Taq Kit) with human androgen receptor primers sense (SEQ ID NO:15) 5'-TCCAGAATCTGTTCCAGAGCG-3' and antisense (SEQ ID NO:16) 5'-TTCGGATACTGCTTCCTGC-3'to yield a 281bp product. To verify the quality of RNA/cDNA preparation, PCR amplification was carried out with human β-actin primers (Promega, UK). To verify that PCR product were not amplified from residual DNA left in RNA samples, an RT negative control was subjected to β-actin PCR amplification.

Please rewrite the paragraph on page 63, starting with line 12, as follows:

IRE TFO: (SEQ ID NO:17) (5') GGGUGGTGGGGTTGTGTT (3')

Please rewrite the paragraph on page 63, starting with line 25, as follows:

L218: HHHHHH-29aaMAD-DDD-Penetratin (SEQ ID NO:14)
(Link)HHHHHHMNIAMLLEAADYLERREREAEHGYASMLPDDDR QIKIWFQNRRMKWKK(carboxamide)

Please rewrite the first paragraph on page 64 as follows:

L219: DDD-29aaMAD-HHHHHH-Penetratin

(SEQ ID NO:18)

(Link)DDDMNIAMLLEAADYLERREREAEHGYASMLPHHHHHHHRQIKIWFQNRRMKWKK

(carboxamide)

Please rewrite the paragraph starting at line 14 on page 70 as follows:

(SEQ ID NO:19) 5'- TCCAGAATCTGTTCCAGAGCG -3'

Please rewrite the paragraph starting at line 16 on page 70 as follows:

(SEQ ID NO:20) 5'- TTCGGATACTGCTTCCTGC -3'

Please rewrite the two paragraphs starting at line 18 on page 70 as follows:

ß-actin Forward primer: (SEQ ID NO:21) 5'-TTTTCGCAAAAGGAGGGGAG-3'

ß-actin Reverse primer: (SEQ ID NO:22) 5'-AAAGGCAACTTTCGGAACGG-3'

Please rewrite the last paragraph on page 71 and the first four paragraphs on page 72 as follows:

The peptide portion of the molecule may have a nuclear localisation signal (NLS) to target the molecule to the nucleus. The peptides used in this example are:

a) DDD-MAD1-DDD-NLS,

which has the amino acid sequence:

(SEQ ID NO:23)

(Link)DDDMNIQMLLEAADYLERREREAEHGYASMLPDDDPKKKRKV (carboxamide)

and,

b) DDD-NLS-DDD-MAD1,

which has the amino acid sequence:

(SEQ ID NO:24)

(Link)DDDPKKKRKVDDDMNIQMLLEAADYLERREREAEHGYASMLP (carboxamide)

The NLS is a 7 amino acid (sequence (SEQ ID NO:25) PKKKRKV) functional nuclear localisation signal derived from the SV40 T-antigen.